

REMARKS

Claims 1-15 are currently pending. Claims 5-6, 12-13 and 15 are amended. Support for the amendments is seen in original claim 1 and throughout the specification. No new matter has been introduced into the application by way of amendment.

Rejection under 35 USC 112, second paragraph:

(a) Claims 1-15 are rejected as being ambiguous drawn to the term tiotropium because a search of Registry resulted in eight different compounds. Applicants respectfully traverse. Applicants are claiming one or more salts of tiotropium. Tiotropium is has a specific structure and the salts thereof is probably what the Examiner found while searching on registry. The fact that the Examiner found a definite amount of compounds should lead one to conclude that the term is not ambiguous but in fact is definite and clearly pointed out and distinctly claimed. Therefore, withdrawal of the rejection is respectfully requested.

(b) Claims 5-6 and 9-13 are being rejected as being ambiguous. Applicants have amended the claims to remove any ambiguity from the claims rendering the rejection moot.

Withdrawal of the rejection is respectfully requested.

Rejection under 35 USC 103(a):

Claims 1-15 are rejected as being unpatentable over WO 00/75114 in view of WO 02/45703. Applicants respectfully traverse. The Examiner has failed to present a prima facie case of obviousness.

The Examiner asserts that '114 teaches compounds of formula (1) that encompass the instantly claimed formula 2' in combination with other active ingredients such as tiotropium bromide to treat obstructive airway diseases for use as an inhalant or solid drug. The Examiner further asserts that any difference between '114 and the instant claims such as (a) '114 not teaching the instantly claimed compounds of formula 2' and (b) weight ratios, inhalable powders or propellants, is mitigated by the teachings of '703. The Examiner asserts that '703 teaches the compounds of formula 2' in combination with a corticosteroid and teaches propellants, inhalable forms, dispersions, nebulizers, particle size and weight ratios. Hence, the Examiner asserts that one of ordinary skill in the art would be motivated to

prepare the instant combination because '114 teaches compounds of formula (1) and '703 teaches compounds of formula 2' and the combination of these two references would have been within the skill of the ordinary artisan. Applicants respectfully traverse.

The Examiner is right in that the '114 reference does not specifically exemplify tiotropium salt with any other active ingredient or disclose or exemplify the specific combination with compounds of formula 2' or the weight ratios, inhalable powders or propellants that can be contemplated with tiotropium salt as one of the active ingredients. The Examiner is, however, wrong in asserting that this lack of a teaching and/or suggestion can be resolved by the teachings of '703.

In arriving at the conclusion that the reference renders the instant invention obvious, the Examiner has used hindsight reconstruction or, at best, established that it would have been "obvious to try" various combinations. *In re Geiger*, 815 F. 2d 686 at 688, 2 USPQ2d at 1278, held that this standard is in error in circumstances where it is alleged that varying all parameters where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.

Similarly, in preparing a combination product, there requires several parameters to be present, such as concentration, pH conditions, choice of active ingredients, complexing agents, stabilizers, co-solvents, adjuvants and additives, which result in numerous possibilities of choices to arrive at a particular combination. The specific teachings in the '703 reference are drawn to using compounds of formula 2' as the active ingredient in the composition, the examples of preparing, the complexed co-active ingredient (corticosteroid), solvents, concentrations and pH conditions are all drawn to the compound of formula 2' composition. Nowhere in the reference is it taught or suggested that tiotropium salt may be complexed with co-active ingredient selected from compounds of formula 2', in a weight ratios and dosages as instantly claimed and that such a combination of possible choices is likely to be successful. '703 does not provide any suggestion or teaching to narrow these numerous possibilities that are disclosed therein that would render the instantly claimed composition obvious. "Obvious to try", is not the standard under section 103.

Applicants assert that there no teaching or suggestion to motivate one of ordinary skill in the art to prepare the composition as instantly claimed.

AMENDMENT
U.S. Appln. No. 10/717,868

Assuming arguendo that the Examiner presented a prima facie case of obviousness, the instantly claimed combination has unexpected properties. The unexpected activity of the combination is shown in the declaration filed under 37 CFR 1.132, attached. The combination is significantly more potent than the use of each active ingredient alone and the synergistic effect is even greater than the calculated sum of the effects of each single component administered alone. In view of the arguments presented above and the declaration attached, Applicants believe that the rejection as provided lacks merit and withdrawal of the rejection is respectfully solicited.

In view of the above amendments and remarks, Applicants respectfully submit that this application is now in condition for allowance and earnestly request such action.

If any points remain at issue which can best be resolved by way of a telephonic or personal interview, the Examiner is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,



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